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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/775,554	02/09/2004	Meng Yang	312762004400	6701

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
09/02/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/775,554	YANG ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response received on 4/15/10 has been entered. Claims 1-3 are currently pending and under examination. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in a previous office action.

Claim Rejections - 35 USC § 103

The rejection of claims 1-3 under 35 U.S.C. 103(a) as being unpatentable over Okabe et al. (1997) FEBS Lett., Vol. 467, 313-319, in view of WO 02/28188 A1 (4/1/02), hereafter referred to as Kern, and Yang et al. (2002) PNAS, Vol. 99(6), 3824-3829, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant reiterates their arguments previously submitted against the teachings of Okabe et al. and Kern et al. In particular, the applicant argues that Kern et al. teaches inducible promoters and that while constitutive promoters are mentioned in the alternative, it is not expressly stated that these promoters provide expression in all tissues as recited in the instant claims. In addition, the applicant argues that Kern et al. doesn't teach the four step process recited in the instant claims for producing the mouse which applicants contend is necessary for a stable phenotype.

In response, it is first noted that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references.

See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Okabe et al., the primary reference, was cited for teaching the production of a transgenic mouse comprising a transgene encoding GFP under control of the constitutive chicken beta-actin promoter (Okabe et al., page 313). Okabe et al. teaches that GFP was expressed in all tissues of the transgenic mouse with the exception of erythrocytes and hair (Okabe et al., page 313). Okabe et al. further teaches that the transgenic mice expressing GFP can be used as a model of tumorigenesis by implanting non-green tumor cells into the 'green mice' (Okabe et al., page 319, column 2). Kern et al. was cited to supplement the teachings of Okabe et al., and Kern et al. specifically teaches the embodiment of a transgenic animal where a marker such as GPF is constitutively expressed (Kern et al., page 13, paragraph 1). It does not matter that Kern et al. also teaches to use an inducible promoter as a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also *Celeritas Technologies Ltd. v. Rockwell International Corp.*, 150 F.3d 1354, 1361, 47 USPQ2d 1516, 1522-23 (Fed. Cir. 1998). Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). In addition, there is no requirement that Kern et al. teach that expression of a marker protein such as GFP using a constitutive promoter will result in expression of the transgene in all tissues except hair and erythrocytes since the primary reference, Okabe et al., supplies this teaching.

As for the steps used to product the transgenic mouse, it is again reiterated that the claims are product by process claims. The applicant is reminded that "[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted). Second, the applicant is arguing limitations that are not present in the claims. The claims as written contain no limitations regarding the stability of the rodent as a final product or the stability of the rodents produced during any one of the breeding steps. Further, there is no evidence of record that the mouse product produced using four crossings as set forth in the claims is structurally different from that disclosed and suggested by Kern, using the Okabe et al. GFP transgenic mouse as a starting point. It has also been noted in previous office actions that Kern et al. specifically teaches methods of making a mouse as claimed by stably integrating the detectable gene into the chromosome of a mouse embryonic stem cell and using the embryonic cell to develop strains of homozygous mice having two copies of the integrated construct in every cell, and then breeding the mice with nu/nu mice to produce mice that are homozygous for the transgene and homozygous for immunodeficiency. As noted previously, the guidance provided by Kern is in fact more detailed than that provided by the instant specification for making transgenic mice. Thus, it is maintained that a skilled artisan reading both Okabe et al. and Kern et al. would find ample motivation to cross the GFP expressing mice of Okabe et al. with a nude mouse

according to the teachings of Kern et al. to produce an immunocompromised mouse which expresses GFP in all tissues expect hair and erythrocytes.

The applicant further argues that Kern et al. teaches a different use for the transgenic mice than as a mouse model for tumor growth and metastasis and that Okabe et al., while teaching to implant non-green tumor cells into a green mouse, does not teach how this model would be used or why the green background would be helpful. In response, the claims, as noted above, are product claims, not method claims. Further, the claims as written do not recite any particular intended use, and even if they did, the applicant is reminded that the use of a product for a particular purpose is not afforded patentable weight in a product claim where the body of the claim does not depend on the preamble for completeness but, instead, the structural limitations are able to stand alone. The MPEP states that,".. in apparatus, article, and composition claims, intended use must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art." *In re Casey*, 152 USPQ 235 (CCPA 1967); *In re Otto* , 136 USPQ 458, 459 (CCPA 1963)(MPEP 2111.02). As set forth in the rejection of record, it is maintained that based on the motivation to implant a non-green tumor into GFP expressing transgenic mice provided by Okabe et al., and the teachings of Yang et al. that RFP expressing xenogenic tumors are readily detectable in nude mice and that dual-color imaging allows for the detection of both RFP and GFP expressing cells in the same mouse, it would have been *prima facie* obvious to the skilled artisan at the time of filing to implant an RFP expressing tumor xenograft into a GFP nude mouse with a reasonable expectation of success in both making the mouse as claimed and in visualizing both GFP and RFP expressing cells within the mouse.

In regards to the teachings of Yang et al., the applicant argues that Yang et al. only teaches dual color imaging in the context of separately implanted green and red tumors and does not suggest providing a green mouse as a backdrop to a red tumor. In response, Okabe et al. was cited for teaching to implant a non-green tumor into a green mouse. Yang et al. was cited for teaching that rat tumors cells transformed to express the gene for red fluorescent protein (RFP) can be transplanted into nude mice and are easily detectable (Yang et al., pages 3825, and 3827-3828). Yang et al. further teaches that both GFP and RFP expressing cells in a nude mouse can be visualized at the same time using dual color imaging (Yang et al., pages 3827-3829). Thus, the skilled artisan, having been provided the suggestion by Okabe et al. to implant a non-green tumor into a green mouse, and having been taught by Yang et al. that red expressing tumor cells can be transplanted into nude mice and differentially detected from green tissue in the form a second green tumor, would have found ample motivation to implant a red fluorescent protein expressing tumor as the non-green tumor into an immunocompromised green mouse as taught by Okabe et al. in view of Kern et al.

Therefore, for the reasons set forth above, the rejection of record stands.

The rejection of claims 1-3 under 35 U.S.C. 103(a) as being unpatentable over Okabe et al. (1997) FEBS Lett., Vol. 467, 313-319, in view of WO 02/28188 A1 (4/1/02), hereafter referred to as Kern, and Verkhusha et al. (2001) J. Biol. Chem., Vol. 276(32), 29621-29624, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant has not provided separate arguments for this rejection with the exception of particular arguments directed to the teachings of Verkhusha et al. The arguments made against the teachings of Okabe et al. and Kern et al. have been addressed in detail above and have not been found persuasive.

In regards to Verkhusha et al., the applicant argues that this reference is irrelevant to the instant invention as Verkhusha et al. teaches methods to judge the maturity of cells and tested the differential detection of GFP and mutant RFP in *Drosophilia* cells, not rodents as instantly claimed. In response, and as noted above, the claims are product claims, not method claim; and since the intended use for the claimed rodents disclosed in the specification does not result in a structural difference between the claimed invention and the prior art, it has no patentable weight. Further, Okabe et al. was cited for specifically teaching to implant a non-green tumor into a green mouse. Verkhusha et al. was cited for teaching a variant of RFP with increased fluorescence which can be used to label cells and which has improved properties for dual color imaging with GFP expressing cells (Verkhusha et al., pages 29621-29622). Thus, the skilled artisan, having been provided the suggestion by Okabe et al. to implant a non-green tumor into a green mouse, and having been taught by Verkhusha et al. that a variant of RFP can be used to label cells and differentially detected from GFP expressing cells, would have found ample motivation to implant a variant red fluorescent protein expressing tumor as the non-green tumor into an immunocompromised green mouse as taught by Okabe et al. in view of Kern et al.

Therefore, for the reasons set forth above, the rejection of record stands.

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related

to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633